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Pesticide Fact Sheet Number 228: Triflumizole

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This document contains up-to-date chemical information, including a summary of the Agency's regulatory position and rationale, on a specific pesticide or group of pesticides. A Fact Sheet is issued after one of the the following actions has occurred.

1. Issuance or reissuance of a registration standard,
2. Issuance of each special review document,
3. Registration of a significantly changed use pattern,
4. Registration of a new chemical, or
5. An immediate need for information to resolve controversial issues relating to a specific chemical or use pattern.

17. Document Analysis a. Descriptors

Pesticides, regulations, Chemical Information Fact Sheet, Use Patterns, science findings.

b. Identifiers/Open-Ended Terms

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Pesticide Fact Sheet

PB92-126978

Name of Chemical: 1-[1-[[4-chloro-2(trifuoromethyl)phenyl]imino] -2-propoxyethyl]-1H-imidazole

Reason for Issuance: Registration of New Active Ingredient

Date Issued: 10-24-91

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DESCRIPTION OF CHEMICAL

Generic Name: 1-[1-[[4-chloro-2-(trifluoromethyl)phenyl]imino]-2-propoxyethyl]-1H-imidazole
Common Name: Triflumizole
Trade Name: Terraguard
EPA Shaughnessy Code: 128879
Chemical Abstracts Service (CAS) Number: 68694-11-1
Year of Initial Registration: 1991
Pesticide Type: Fungicide
U.S. and Foreign Producers: Uniroyal Chemical Company, Inc.
74 Amity Road
Bethany, CT 06525

USE PATTERNS AND FORMULATIONS

APPLICATION SITES: The manufacturing use product (MP) is for use only in the formulation of fungicides. The end-use product is for use in control of Cylindrocladium root and petiole rot on Spathiphyllum.

TYPES OF FORMULATION: The technical grade is a white crystalline formulation containing 97% active ingredient. The end-use product is a wettable powder containing 50% active ingredient.

TYPES AND METHODS OF APPLICATION: The end-use product is a protectant fungicide to be used as a soil drench, foliar spray or through chemigation for control of diseases on ornamentals grown in enclosed commercial structures such as greenhouses, shade houses and interior scapes.

APPLICATION RATES: For all methods of treatment for Terraguard (soil drench, foliar spray and/or chemigation), the pesticide is applied at the rate of 4 to 8 oz. per 100 gallons of water. This treatment is repeated every 2 to 4 weeks or as needed. For best results use sufficient volume to ensure adequate soil penetration.

SCIENCE FINDINGS

Summary Science Statement

Available acute toxicity studies indicate that triflumizole is in Toxicity Category I (Danger) based on the primary eye irritation study with rabbits.

Chronic feeding/oncogenicity studies were conducted in both the rat and mouse. The chronic feeding study in the rat suggests that the liver is the main target organ with the ovary and kidney as secondary target organs. Although there was an accompanying increase in organ weights, no carcinogenic effects were seen.

In the chronic feeding study in mice, the results of blood chemistry, organ weights and gross and histological examinations also indicate the liver as the target organ.

Triflumizole did not induce either genotoxic effects or chromosomal aberrations in a series of mutagenicity studies.

The teratology studies were conducted in the rabbit and rat. In the rat studies, incidences of dilatation of the renal pelvis and increased 14th rudimentary ribs were seen. In the rabbit, an increase in postimplantation losses was noted.

Environmental fate data indicate that triflumizole has low potential for leaching. Aerobic soil metabolism data indicates that triflumizole is degraded rapidly by soil microbes to several products of which one is CO_2. Hydrolysis data show that the parent compound is quite stable at near neutral pHs and undergoes slow hydrolysis at either mild acidic or basic conditions. Studies also show that triflumizole has a half-life of 18 days in sandy loam soil under laboratory conditions.

Ecological studies indicate triflumizole is practically non-toxic to honeybees and birds. Triflumizole is categorized as being moderately toxic to highly toxic to fish. Since this is a minor use registration and since greenhouse applications have been traditionally treated as indoor uses, the hazards to nontarget species and endangered species are considered to be minimal.

TOXICOLOGICAL CHARACTERISTICS

Acute Toxicity

Acute oral toxicity in rats:	LD_{50} 2.43 g/kg males LD_{50} 2.05 g/kg females Toxicity Category III
Acute dermal toxicity in rats:	LD_{50} > 2000 mg/kg Toxicity Category III
Acute inhalation toxicity in rats:	LC_{50} > 3.2 mg/L Toxicity Category III
Primary eye irritation in rabbit:	Ocular opacity; Toxicity Category I
Primary dermal irritation in rabbit:	Negative; No irritation observed; Toxicity Category IV
Dermal sensitization in guinea pigs:	Positive for contact sensitization

CHRONIC STUDIES

Rodent Feeding/Oncogenicity

A 2-year feeding/oncogenicity study with Sprague-Dawley rats was conducted. Rats were fed 0, 5, 20 or 80 mg/kg/day doses of triflumizole equivalent to 0, 100, 400 and 1600 ppm triflumizole for 104 weeks with an interim sacrifice at 52 weeks. Numerous organ weights, clinical chemistry and hematology parameters and microscopic changes indicate the main target organ is the liver, with fatty vacuolization and periacinar hepatic hypertrophy seen at all dose levels tested. Ovarian organ weights as well as well-developed follicles indicate the ovary as a target. Kidney weights were affected as well with increased cortical cysts seen in the kidneys of mid and high dose animals. The NOEL is < 100 ppm, based on fatty vacuolization and periacinar hepatic hypertrophy seen at all dose levels tested. An increase in tumor incidence was not noted in any treatment groups.

A 2-year feeding/oncogenicity study with male and female mice using dietary concentrations of 0, 100, 400 and 1600 ppm equivalent to 0, 15, 60 and 240 mg/kg/day was conducted. There were interim sacrifices at 26, 54, 78 and 104 weeks. Major effects were seen in the liver at all doses tested. Clinical chemistry changes reflecting liver toxicity included changes in alkaline phosphatase, BUN, SGOT, SGPT and cholesterol. Absolute and relative liver weights were increased at all time periods in the high dose males and females and in some animals of the mid dose groups. At sacrifice, liver changes in all dose groups included hepatic nodules and cytoplasmic alterations. The systemic NOEL was less than 100 ppm. Although there was a slight

increase the incidence of lymphoma in both treated males and females, it was judged not be compound-related.

A 3-month feeding study in rats was conducted using dietary concentrations of 0, 20, 200 and 2000 ppm equivalent to 0, 2, 20 and 200 mg/kg/day. The NOEL was 200 ppm. The LEL was 2000 ppm (HDT) based on slight decrease in food consumption and body weight and changes in blood chemistry.

A 3-month feeding study with mice was conducted using dietary concentrations of 0, 20, 200 and 2000 ppm equivalent to 0, 3, 30, 300 mg/kg/day. The NOEL was 200 ppm and the LEL was 2000 ppm based on liver effects.

A 30-day feeding study with rats was conducted using dietary concentrations of 20, 200 and 2000 ppm equivalent to 0, 2, 20 and 200 mg/kg/day. The NOEL was 200 ppm and the LEL was 2000 ppm based on liver changes, necrosis and fatty metamorphosis.

A 30-day feeding study with mice was conducted using dietary concentrations of 20, 200 and 2000 ppm equivalent to 0, 3, 30 and 300 mg/kg/day. The NOEL was 200 ppm and the LEL was 2000 ppm based on enlarged livers.

Non-Rodent Feeding Studies

A 1-year feeding study with beagle dogs using dietary concentrations of 0, 100, 300 and 1000 ppm equivalent to 0, 2.5, 7.5 and 25 mg/kg/day was conducted. The NOEL was 300 ppm and the LEL was 1000 ppm based on liver and blood chemistry changes.

TERATOLOGY

A teratology study using Sprague-Dawley rats was conducted by administering levels of 0, 10, 35 and 120 mg/kg/day by gavage. The teratogenic NOEL was > 120 mg/kg/day (HDT). The maternal NOEL in this test was 10 mg/kg/day and maternal LEL was 35 mg/kg/day based on decreased body weight and decreased water and food consumption. The fetotoxic NOEL was < 10 mg/kg/day (LDT) based on dilation of renal pelvis.

A complementary study was conducted using dose levels of 0 and 3 mg/kg; the NOEL was 3 mg/kg. Another teratology study using rats was conducted using dose levels of 0, 3, 7, and 35 mg/kg by gavage. The maternal NOEL was 7 mg/kg. The maternal LEL was 35 mg/kg based on reduced body weight gain and decreased food consumption. The developmental NOEL was 7 mg/kg. The developmental LEL was 35 mg/kg based on death and increase in incidence of 14th rudimentary ribs and cervical ribs. The A/D ratio was determined to be 7/7 = 1.

A teratology study was conducted in rabbits by administering dosage rates of 0, 50, 100 and 200 mg/kg by gavage. The maternal NOEL was 50 mg/kg. The maternal LEL was 100 mg/kg based on decreased food consumption, body weights and organ weights. The

developmental NOEL was < 50 mg/kg (LDT) based on decreases in fetal and placental body weights and 24-hour survivals. The A/D ratio was determined to be 50/< 50 = > 1. A range finding study was conducted in rabbits using dose rates of 0, 10, 50, 100, 200 and 300 mg/kg by gavage. The maternal NOEL was 100 mg/kg. The maternal LEL was 200 mg/kg based on decreased body weight and food consumption. The developmental NOEL was 100 mg/kg. The developmental LEL was 200 mg/kg based on increased postimplantation losses.

Another teratology study was conducted in rabbits using lower doses (0, 5, 25 and 50 mg/kg by gavage). There was no evidence of clear maternal toxicity. The offspring showed no adverse effects. The maternal NOEL was > 50 mg/kg and the developmental NOEL was > 50 mg/kg/day.

REPRODUCTION

In a 2-generation rat reproduction study, dose levels of 0, 30, 70 and 170 ppm in feed were used. No parental toxicity was observed. The parental NOEL was > 170 ppm (HDT). The reproductive NOEL was 70 ppm. The reproductive LEL was 170 ppm based on increased gestation lengths. The developmental NOEL was 70 ppm. The developmental LEL was 170 ppm based on reduced F1a litter size and increased fetal incidences of hydroureter and space between body walls and organs.

In a 3-generation rat reproduction study, dose levels of 0, 70, 170 and 420 ppm in feed resulted in a NOEL < 70 ppm (LDT) based on increased gestation length. At 170 ppm, there was pup mortality. At 420 ppm, there was reduced body weight gain, increased length of estrous cycles, reduced vaginal cornification, extended gestation length and high pup mortality.

Another 3-generation rat reproduction study was conducted using lower dose levels (0, 30, 70 and 170 ppm). The reproduction NOEL was < 30 ppm based on increased gestation lengths at all doses tested. The developmental NOEL was 70 ppm. The developmental LEL was 170 ppm based on increased incidence of hydroureter and space between the body wall and organs, increased pup mortality and reduced pup weight. The parental NOEL was > 170 ppm (HDT).

MUTAGENICITY

Triflumizole was negative for mutagenicity in the mitotic gene conversion test, rec assay test, in vitro mouse micronucleus test, reverse mutation in Salmonella and E. coli test and unscheduled DNA synthesis test.

ENVIRONMENTAL FATE

Environmental fate studies for leaching/adsorption/desorption show that unaged [^{14}C] triflumizole was slightly mobile in a column (30.4 cm length) of sandy soil treated with 214 ug (1 lb ai/A) of phenyl ring-labeled [^{14}C] triflumizole (radiopurity 93.4%) and leached with 63.7 column CM of distilled water. Seventy-eight percent of the recovered radioactivity was found in the top six inches of soil. The majority (> 81%) of the radioactivity in each soil segment was triflumizole. This, together with the leachate data, indicates low potential for leaching and indicates that triflumizole should not pose a problem in field runoff or in contamination of ground water.

Data from an aerobic soil metabolism study of ^{14}C triflumizole in sandy loam soil indicate that triflumizole underwent soil degradation with a half-life of 18 days. The parent compound degraded via three degradation intermediates to 4-chloro-2-trifluoromethylaniline, which volatilized from the soil and/or underwent further degradation to CO_2 by microorganisms.

Hydrolysis studies show that phenyl-labeled [^{14}C] triflumizole (radiochemical purity > 99%), at 5 ppm, degraded in sterile aqueous 0.01 M buffered solutions with half-lives of 7 to 15 days at pH 5, > 30 days at pH 7 and 3 to 17 days at pH 9 when incubated in the dark at 25 $\pm$ 1 C. The registrant-calculated half-lives were 8 to 9 days (pH 5), 64.6 days (pH 7) and 3.9 days (pH 9). At 30 days posttreatment, [^{14}C] triflumizole accounted for 73.5% of the applied radioactivity in the pH 7 solution. 4-Chloro-alpha-alpha-alpha-trifluoro-N-2-propoxyacetyl-0-toluidine was identified as the major degradate at all three pHs, with maximum concentrations of 83.1% of the applied at pH 5, 20.8% at pH 7 and 84.0% at pH 9. Material balances ranged from 96 to 103% during the test period.

ECOLOGICAL CHARACTERISTICS

Studies submitted show that triflumizole is practically nontoxic to honeybees (LD_{50} > 160 ug per bee) and birds (LC_{50} > 5,620 ppm and LD_{50} > 2,510 ppm). Since it is unlikely that triflumizole will come into contact with these species, it is not expected to pose a threat to honeybees and birds (nontarget and endangered species). Triflumizole is categorized as being moderately toxic to highly toxic to fish. The expected levels of triflumizole in a farm pond are not predicted to exceed 1/10 of the warmwater fish LC_{50} (1.2 ppm) which is the nontarget species cutoff point. There are only two endangered fish species in Florida. The shortnosed sturgeon (Acipenser brevinostrum) is in Duval and Putnam Counties.

The Okaloosa darter (Etheostoma okaloosae) is in Walton and Okaloosa Counties. None of these four counties is in southern Florida where the pesticide will be used. The expected levels of triflumizole in a farm pond are not predicted to exceed 1/20 of the warmwater fish LC_{50} (1.2 ppm) which is the endangered species cutoff point. Triflumizole is not expected to be a threat to endangered fish. Since this is a minor use registration and greenhouse applications have been traditionally treated as indoor uses, the hazards to non-target species and endangered species is considered to be minimal. All available ecological data indicate that the use of triflumizole on Spathiphyllum will not cause undue environmental damage.

BENEFITS

This chemical has low mammalian toxicity. Its use as a fungicide on ornamentals does not pose any unreasonable effect to man or the environment. Triflumizole is effective at low rates in controlling Cylindrocladium.

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